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Comments on the

Nomination to hold a workshop on Alternative Methods to replace the mouse LD_{50} assay for Botulinum toxin potency testing issued by NICEATM

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ad (1) Information on development and/or validation activities

The Institute for Applied Biotechnology is currently involved in two developments for botulinum neurotoxin potency testing: One method aimes to quantify the peptide cleavage activity in all liquid laser desorption ionization, the second approach is a cell culture based assay, which measures the biological activity of the neurotoxins as a whole (heavy and light chain).

ad (2) Comments on the appropriateness and priority of a workshop

Currently several approaches for BoNT potency testing are under development, which have the potential to replace or at least refine the mouse bioassay. Urgent action is needed to identify the most promising techniques and the applications for them. R&D activities, in-process control and batch release testing of BoNT in therapy and cosmetics do not necessarily need the same methods as testing of clinical, food or environmental samples. However, alternative methods suitable for a variety of applications would merit the validation work with BoNT products, but with detection/diagnostic evaluations of other sample matrices as well. To conclude, a workshop would offer the unique opportunity to move forward in refining/replacing the mouse bioassay and should be given high priority.

ad (4) Submission of data from mouse LD_{50} botulinum potency testing

With approx. 3000 mouse bioassays per year, the Institute for Applied Biotechnology has gained experience in BoNT potency testing with human, veterinary, food and environmental samples, but also with BoNT preparations of various purities (culture supernatant, toxin complex, 150 kD toxin) and of almost all types (A to F). A

considerable effort is needed to carefully check and analyse the data. Thus the evaluation and the raw data can not be supplied by March, 13th, but would be available at a later stage.